A Proteomic Study of Resistance and Susceptibility to Schistosome Infecton in *Biomphalaria glabrata*

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I certify that except where indicated, all material in this thesis is the result of my own investigation and references used in preparation of the text have been cited. The work has not previously been submitted as part of any other assessed module, or submitted for any other degree or diploma.

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ABSTRACT

Despite current control programmes approximately 200 million people are infected with schistosomes, of which 20 million suffer severe illness, and 120 million are symptomatic. It has been suggested that to control the parasite it is necessary to control the intermediate host, *B. glabrata.*

Although some *B. glabrata* isolates are naturally resistant to *S. mansoni*, the mechanisms underpinning resistance remain unclear. It is expected that unraveling both host and parasite gene expression might eventually lead to novel methods of disease control, such as a 'genetic control technique' which sets out to interrupt the life cycle of schistosomes in the field by increasing the proportion of genetically resistant intermediate host snails.

In this investigation two populations of *B. glabrata*, one susceptible and one resistant, where challenged by infection with *S. mansoni*. The hepatopancreas organ, the site of sporocyst development, was dissected and its proteome examined using 2D gel electrophoresis, allowing comparison between susceptible and resistant proteomes. Unique spots of interest were analysed by mass spectrometry and bioinformatics, to identify the proteins.

Of the 302 protein spots from the susceptible snail gel matched with spots on the resistant snail gel, 110 and 105 spots showed up- and down-regulation of more

than two fold respectively, possibly indicating significant change in expression of resistant snail proteins compared with susceptible snail proteins.

The resistant snail sample contained more unique spots (273), than the susceptible sample (15), which may be involved in an immune response against *S. mansoni*. The fragmentation spectra produced, of unique spots of interest from the resistant snail gel, were of poor quality due to limitations of mass spectrometry. Proteins with possible immune functions were identified by PMF through MASCOT, although no matches were significant.

Future work would involve further mass spectrometry to yield more accurate results leading to a better understanding of the components of the proteome of the hepatopanceas. The project has highlighted many points of interest to investigate and has emphasized the many gaps in our understanding.

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TABLES AND FIGURES

ABBREVIATIONS

2D PAGE	Two Dimensional Polyacrylamide Gel Electrophoresis
2DE	Two Dimensional gel Electrophoresis
AIDS	Acquired ImmunoDeficiency Syndrome
CAN	Acetonitrile
CHAPS	[(3-Cholamidopropyl)dimethylammonio]-1-propanesulfonate
C-terminal	Carboxyl-terminal of amino acid or peptide
BLAST	Basic Local Alignment Tool
BSA	Bovine Serum Albumin
cm	Centimetre
ddH_2O	Double distilled water
Da	Dalton
DTT	1,4-dithiothreitol
E-value	Expectancy Value
FREP	Fibrogen Related Protein
H_2O_2	Hydrogen Peroxide
HIV	Human Immunodeficiency Virus
IEF	Isoelectric Focusing
MALDI ToF	Matrix Assisted Laser Desorption Ionisation Time of Flight
ml	Millilitre
MnSOD	Manganese Superoxide Dismutase
MOWSE	Molecular Weight Search
mRNA	Messenger Ribonucleic Acid
MS	Mass Spectrometry
MS-MS	Tandem Mass Spectrometry
MW	Molecular Weight
NCBI	National Centre for Biotechnology Information
NO	Nitric Oxide
N-terminal	Amino-terminal of amino acid or peptide
PAGE	Polyacrylamide Gel Electrophoresis
PMSF	Phenyl Methyl Sulfonyl Fluoride
pI	Isoelectric Point
PMF	Peptide Mass Fingerprint
Q-ToF	Quadruple Time of Flight
SDS-PAGE	Sodium Dodcyl Sulphate Polyacrylamide Gel Electrodes
TFA	Trifluoroacetic acid
TGS Buffer	Tris-Glycine-SDS Buffer
TIF	Tagged Image Files
Tris	Tris(hydroxymethyl)aminomethane
UPPA	Universal Protein Precipitation Agent
UV Ultra	Ultra Violet
V	Volts
WHO	Wold Health Organisation